parameters were obtained (i.e., mean tumour-to-brain ratios (TBR), time-to-peak values). Diagnostic accuracies of PET parameters were evaluated by receiver-operating-characteristic analyses using the clinical follow-up or neuropathological findings as reference. RESULTS: A TBR threshold of 1.95 differentiated BM relapse from treatment-related changes with an accuracy of 85% (P=0.003). Metabolic Responders to ICI or TT on FET PET had a significantly longer stable follow-up (threshold of TBR reduction relative to baseline, ≥10%; accuracy, 82%; P=0.004). Furthermore, at follow-up, time-to-peak values in metabolic responders increased significantly (P=0.019). CONCLUSIONS: FET PET may add valuable information for treatment monitoring in BM patients treated with ICI or TT.

33. SYSTEMATIC REVIEW AND META-ANALYSIS OF BREAST CANCER BRAIN METASTASIS AND PRIMARY TUMOR RECEPTOR EXPRESSION DISCORDANCE

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BACKGROUND: Discordance in hormone receptor (estrogen [ER] and progesterone [PR]) and human epidermal growth factor receptor2 (HER2) status between the primary tumor and brain metastases and its effect on tumor classification subtype switching has been described but remains understudied. METHODS: Using the PRISMA guidelines, a systematic review was performed of series published prior to April 2020 of biopsied or resected breast cancer brain metastasis (BCBM) from the Medline database using the keywords "breast cancer" and "brain metastasis" combined with "estrogen receptor/ER," "progesterone receptor/PR," "HER2/neu," and "receptor conversion/dis- or concordance." Weighted random effects models were used to calculate pooled estimates. RESULTS: Fifteen full-text articles met inclusion criteria and cumulatively reported on 1373 patients who underwent biopsy or resection of at least one BCBM to compare to their primary tumor. At initial diagnosis, receptor expression profiles were 45.0% ER+, 41.0% ER-, 31.0% PR+, 51.0% PR-, 35% HER2+, and 47.0% HER2-. Corresponding receptor expression profiles from the BCBM were 19.0% ER+, 31.0% ER-, 13.0% PR+, 40.0% PR-, 21.0% HER2+, and 26.0% HER2-. Intra-patient receptor discordance comparisons revealed that 540 patients (42.6%) exhibited discordance in any receptor with 17.0% (95% CI: 13.0%-23.0%) discordance for ER status, 23.0% (95% CI: 18.0%-30.0%) for PR status, and 12.0% (95% CI: 8.0%-16.0%) for HER2 status. The most common receptor discordance events found in BCBM compared to primary tumors were ER loss 11.0% (95% CI: 8.0%-16.0%), PR loss 15.0% (95% CI: 11.0%-21.0%), and HER2 gain 9.0% (95% CI: 7.0%-11.0%). CONCLUSIONS: BCBM commonly exhibit receptor expression changes on comparison to primary tumors including a 10% HER2 gain rate, a potential actionable target. Classification patterns need to be updated to reflect changes in overall tumor subtype grouping and which factors predict for BCBM/primary tumor discordance. Overall, tumor subtype switching and its effect on clinical management remains underappreciated.

34. TARGETED THERAPY FOR HER2-POSITIVE BREAST CANCER BRAIN METASTASES: A SYSTEMATIC REVIEW AND META-ANALYSIS

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INTRO: One in three women with HER2-positive breast cancer will develop brain metastases, or intracranial metastatic disease (IMD). Historically, treatment of IMD has been confined to surgery and radiotherapy, with a limited role for chemotherapy. However, recent interest has burgeoned in a role for targeted therapy for treatment of IMD. The lack of high-level evidence, such as meta-analyses, regarding the role of targeted therapy in the management of IMD has prevented its inclusion in guidelines directing treatment. We performed a systematic review and meta-analysis to clarify the role of targeted therapy for IMD in women with HER2-positive breast cancer. METHODS: Following PRISMA guidelines, a search of MEDLINE, CENTRAL, EMBASE, Google Scholar, and grey literature sources was conducted by two independent reviewers. Controlled trials and cohort studies that reported survival, safety, or response outcomes for patients receiving HER2-targeted therapy following IMD diagnosis were included. Meta-analyses using a random-effects model were conducted for OS and PFS. RESULTS: 111 studies reporting on 8226 patients were included. Primary analysis of only RCTs found that HER2-targeted therapy was associated with improved OS (HR 0.63; 95% CI, 0.46–0.86; n = 392) but not PFS (HR 0.75; 95% CI, 0.30–1.85; n = 392) following IMD diagnosis. Secondary analysis combining RCTs and comparative observational studies found that HER2-targeted therapy was associated with improved OS (HR 0.42; 95% CI, 0.35–0.51; n = 2756) but not PFS (HR 0.58; 95% CI, 0.27–1.21; n = 460) following IMD diagnosis. Full analysis will be conducted for all 111 studies for pre-specified outcomes including intracranial PFS. CONCLUSION: These findings support a potential role for HER2-targeted therapy in the management of IMD from HER2-positive breast cancer. Final analysis will synthesize current evidence for outcomes of intracranial response, survival, and safety.

35. EVALUATING CSF CIRCULATING TUMOR DNA IN INTRAPARENCHYMAL BRAIN METASTASIS

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INTRODUCTION: Discordant response between brain and systemic metastases occur in patients receiving targeted therapies and repeat tumor profiling of the progressing site could guide further therapy. We propose that circulating tumor DNA (ctDNA) might be detectable in the cerebrospinal fluid (CSF) and reflective of the genetic profile of intraparenchymal brain metastases. METHODS: Patients with brain metastases undergoing a craniotomy or lumbar puncture were enrolled between July 2018 to April 2019 under an IRB-approved protocol. CSF and blood were collected simultaneously. Cell-free DNA (cfDNA) were extracted and ctDNA were identified and quantified using an Error-Suppressed Deep Sequencing method previously published by our group. Forty-three mutation-prone regions of 24 cancer-associated genes were assayed, and the allelic fractions were calculated against wild-type sequence counts. RESULTS: Sixteen patients were enrolled in this study - 12 patients with intraparenchymal brain metastases, two patients with CSF cytology-positive leptomeningeal disease (LMD) and 2 patients with normal pressure hydrocephalus (NPH) as controls. Primary cancer types were lung (n=10), melanoma (n=2), renal cell (n=1) and colorectal (n=1) cancers. cfDNA was found in all sixteen samples of CSF. CSF ctDNA were found in eight patients (67%) and plasma ctDNA were only found in five patients (42%) with intraparenchymal tumors. In six patients with additional time-matched brain metastasis tissue, four were found to have congruent mutations in the CSF, while only one harbored such mutation in the plasma. DISCUSSION: Analysis of CSF can be a viable alternative to obtaining brain metastasis tissue for DNA profiling in the detection of novel and resistance mutations. The presence CSF ctDNA is not restricted to LMD and were isolated from two-thirds of patients with intraparenchymal disease in our cohort. Furthermore, CSF remains a better source than plasma for the detection of ctDNA across multiple brain metastases tumor subtypes.

36. A PROSPECTIVE TRIAL OF RESECTION PLUS SURGICALLY TARGETED RADIATION THERAPY FOR BRAIN METASTASIS

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INTRODUCTION: Achieving durable local control for larger brain metastases remains problematic. Resection (R) alone is typically insufficient. Even with the addition of stereotactic radiation the 12-month recurrence rate for larger lesions (i.e., >2.5–3 cm) is 20% or more in many series. To improve outcomes we designed and prospectively evaluated a permanently implanted radiation device consisting of Cs-131 seeds positioned within a collagen tile (GammaTile, GT Medical Technologies, Tempe AZ). We combined maximum safe resection and collagen tile brachytherapy (CTBT) with the hypothesis that immediate radiation initiation and/or dose intensification could improve outcomes. MATERIALS/METHODS: From 2013–2018 patients undergoing resection with either previously untreated or recurrent brain metastasis were enrolled on a single arm, multi-histology study (ClinicalTrials.gov, NCT#03088579). At resection completion the tumor bed was lined with collagen tiles imbedded with Cs-131, delivering 60–80 Gy at 5 mm depth. The device was designed to prevent direct source-to-brain contact and to maintain inter-source spacing after closure. No additional local therapy was given unless progression occurred. RESULTS: 16 metastases (12 recurrent/4 previously untreated) in 11 patients were treated. Median diameter 3.1 cm, range 1.9–5.1. Histology was 7 breast, 6 lung, and 3 sarcoma. Median age 60 years; 7 females/4 males. Average time for implantation was 5 minutes. At median radiographic follow-up of 9.5 months (range 0.1–25.2) treatment site progression occurred 1/16 (6%) at 10.9 months. Median treatment site time-to-progression (TTP) has not been reached (95% CI, >10.9 months). Median overall survival (OS) 9.3 months. No surgical adverse events occurred. One patient (6.2%) experienced radiation brain changes and was treated medically. CONCLUSION: R+CTBT demonstrated excellent safety and local control outcomes in this single-arm pre-commercial study. The device recently received FDA clearance for use in newly diagnosed and recurrent brain metastasis. Randomized clinical trials vs standard of care treatments are expected to open in 2020.